CLAIMS

1. A method for inducing a population of T cells to proliferate, comprising:

a) activating a population of T cells; and

b) stimulating an accessory molecule on the surface of the T cells with a ligand which binds the accessory molecule, the activating and stimulating steps thereby inducing proliferation of the T cells.

2. The method of claim 1, wherein the population of T cells is activated by contacting the T cells with an anti-CD3 antibody.

3. The method of claim 1, wherein the population of T cells is activated by contacting the T cells with an anti-CD2 antibody.

4. The method of claim 1, wherein the population of T cells is activated by contacting the T cells with a protein kinase C activator and a calcium ionophore.

5. The method of claim 1, wherein the accessory molecule is CD28.

6. The method of claim 5, wherein the ligand is an anti-CD28 antibody.

7. The method of claim 5, wherein the ligand is a stimulatory form of a natural ligand for CD28.

8. The method of claim 7, wherein the natural ligand is in soluble form.

9. The method of claim 7, wherein the natural ligand is immobilized on a solid phase surface.

10. A method for stimulating a population of T cells to proliferate, comprising

a) contacting a population of T cells with

(1) a first agent which stimulates a TCR/CD3 complex-associated signal in the T cells; and

(2) a second agent which stimulates an accessory molecule on the surface of the T cells.

11. The method of claim 10, wherein the first agent is an anti-CD3 antibody.

12. The method of claim 11, wherein the anti-CD3 antibody is an anti-human CD3 monoclonal antibody.

13. The method of claim 12, wherein the anti-CD3 antibody is immobilized on a solid phase surface.

14. The method of claim 10, wherein the accessory molecule is CD28.

15. The method of claim 14, wherein the second agent is an anti-CD28 antibody.

16. The method of claim 15, wherein the anti-CD28 antibody is an anti-human CD28 monoclonal antibody.

17. The method of claim 10, wherein the second agent is a stimulatory form of a natural ligand for CD28.

18. The method of claim 17, wherein the natural ligand is in soluble form.

19. The method of claim 17, wherein the natural ligand is immobilized on a solid phase surface.

20. The method of claim 13, wherein the solid phase surface further comprises a natural ligand for CD28.

21. The method of claim 11, further comprising:

b) separating the anti-CD3 antibody from the T cells and the second agent;

c) monitoring proliferation of the T cells in response to continuing exposure to the second agent; and

d) restimulating the T cells with the anti-CD3 antibody and the second agent when the rate of T cell proliferation has decreased to induce further proliferation of the T cells.

22. The method of claim 21, further comprising repeating steps (b)-(d) to produce a population of T cells increased in number of from about 100- to about 100,000-fold the original T cell population.

23. The method of claim 22 wherein the second agent is a stimulatory form of a natural ligand for CD28.

24. The method of claim 23, wherein the natural ligand is in soluble form.

25. The method of claim 23, wherein the natural ligand is immobilized on a solid phase surface.

26. The method of claim 25, wherein the solid phase surface is a cell membrane.

27. The method of claim 23, wherein the natural ligand is B7-1.

28. The method of claim 23, wherein the natural ligand is B7-2.

29. A method for stimulating a population of $CD4^+$ T cells to proliferate, comprising:

a) obtaining peripheral blood leukocytes from an individual;

b) isolating a population of $CD4^+$ T cells from the peripheral blood leukocytes by negative selection with a combination of antibodies directed to surface markers unique to the cells negatively selected;

c) contacting the population of $CD4^+$ T cells with an anti-CD3 antibody immobilized on a solid phase and a stimulatory form of a natural ligand for CD28, under conditions appropriate for stimulating proliferation of the T cells;

d) separating the anti-CD3 antibody from the T cells and the natural ligand for CD28;

e) monitoring proliferation of the T cells in response to continuing exposure to the natural ligand for CD28 by examining cell size or determining the level of expression of a cell surface molecule; and

f) restimulating the T cells with the anti-CD3 antibody and the stimulatory form of the natural ligand for CD28 when T cell size has decreased or the level of expression of the cell surface molecule has decreased to induce further proliferation of the T cells.

30. The method of claim 29, further comprising repeating steps (d)-(f) to produce a population of T cells increased in number of from about 100- to about 100,000-fold the original T cell population.

31. The method of claim 30, further comprising genetically transducing the T cells and restoring the transduced T cells to an individual.

32. A method of treating HIV infection in an individual, comprising:

a) obtaining peripheral blood leukocytes from the individual;

b) isolating a population of $CD4^+$ T cells from the peripheral blood leukocytes by negative selection with a combination of antibodies directed to surface markers unique to the cells negatively selected;

c) contacting the population of $CD4^+$ T cells with an anti-CD3 antibody and a stimulatory form of a natural ligand for CD28, under conditions appropriate for stimulating proliferation of the T cells;

d) separating the anti-CD3 antibody from the T cells and the natural ligand fro CD28;

e) monitoring proliferation of the T cells in response to continuing exposure to the stimulatory form of a natural ligand for CD28 by examining cell size or determining the level of expression of a cell surface molecule;

f) restimulating the T cells with an anti-CD3 antibody when T cell size has decreased or the level of expression of the cell surface molecule has decreased to induce further proliferation of the T cells;

g) repeating steps (d)-(f) to produce a population of $CD4^+$ T cells increased in number of from about 10-to about 1000-fold the original T cell population; and

h) restoring the T cells to the individual.

33. The method of claim 32, wherein the natural ligand for CD28 is in a soluble form.

34. The method of claim 32, wherein the natural ligand for CD28 is immobilized on a solid phase surface.

33. The method of claim 32, further comprising rendering the T cells resistant to HIV infection.

34. The method of claim 33, wherein the T cells are rendered resistant to HIV infection by contacting the T cells with at least one anti-retroviral agent which inhibits HIV replication or viral production.

35. The method of claim 33, wherein the T cells are rendered resistant to HIV infection by genetically transducing the T cells to produce molecules which inhibit HIV infection or replication.

36. The method of claim 29, wherein the peripheral blood leukocytes are obtained from an individual afflicted with an immunodeficiency associated with a genetic defect and the method further comprises genetically transducing the T cells to correct for the defect and restoring the T cells to the individual.

37. A method for selectively inducing differentiation of a population of $CD4^+$ T cells into TH1 cells comprising contacting the population of $CD4^+$ T cells with

(1) a first agent which activates T cells; and

(2) an anti-CD28 antibody to selectively stimulate the differentiation of the $CD4^+$ T cells into TH1 cells.

38. The method of claim 37, wherein the first agent stimulates a TCR/CD3 complex-associated signal in the T cells.

39. The method of claim 38, wherein the first agent is an anti-CD3 antibody.

40. The method of claim 39, wherein anti-CD3 antibody is an anti-human CD3 monoclonal antibody.

41. The method of claim 39, wherein the anti-CD3 antibody is immobilized on a solid phase surface.

42. The method of claim 37, wherein the first agent is an anti-CD2 antibody.

43. The method of claim 37, wherein anti-CD28 antibody is an anti-human CD28 monoclonal antibody.

44. A method for selectively inducing differentiation of a population of $CD4^+$ T cells into TH2 cells comprising contacting the population of $CD4^+$ T cells with

(1) a first agent which activates T cells; and

(2) a natural ligand for CD28 to selectively stimulate the differentiation of $CD4^+$ T cells into TH2 cells.

45. The method of claim 44, wherein the natural ligand is in soluble form.

46. The method of claim 44, wherein the natural ligand is immobilized on a solid phase surface.

47. The method of claim 46, wherein the solid phase surface is a cell membrane.

48. The method of claim 44, wherein the natural ligand is B7-1.

49. The method of claim 44, wherein the natural ligand is B7-2.